## REMARKS

Applicant has received and reviewed the Office Action mailed January 23, 2002 (Paper No. 20). Claims 1, 3-11, 13-44, 46, 48-64, 66-74 and 105-107 are currently pending in the application. Of these, claims 105-107 have been allowed; claims 1, 3-11, 13-32, 34-44, 46, 48-62, 64, and 66-73 have been rejected; and the Office has objected to claims 33, 63, and 74.

Reconsideration of the present application is respectfully solicited.

### Allowable Subject Matter

The Office has objected to claims 33, 63, and 74 as being dependent upon rejected claims 30, 57, and 64, respectively, but has indicated that each of these claims recites allowable subject matter. The allowability of the subject matter recited in each of these claims is noted with appreciation.

None of these claims has been amended to independent form because it is believed that, for the reasons provided hereinafter, that each of independent claims 30, 57, and 64 is allowable over the cited references. Accordingly, it is respectfully submitted that claims 33, 63, and 74 are not objectionable because they depend from allowable claims.

The allowance of claims 105-107 is gratefully acknowledged.

### Rejections Under 35 U.S.C. § 103(a)

M.P.E.P. § 706.02(j) sets forth the standard for a Section 103(a) obviousness rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002). The factual inquiry whether to combine references must be thorough and searching and based on objective evidence of record. *Id.* Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *Id.* Even when the level of skill in the art is high, the Office must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination. *Id.* In other words, the Office must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious. *Id.* When the Office relies on what it asserts to be general knowledge to negate patentability, that knowledge must be articulated and placed on the record. *Id.* at 1345. The Office cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies. *Id.*

Isaka in View of Overton

Claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,482,598 to Isaka et al. (hereinafter "Isaka") in view of U.S. Patent 5,611,846 to Overton et al. (hereinafter "Overton"). Applicant respectfully traverses this rejection, as set forth hereinafter.

The Office relies on Isaka as teaching a chromatograph apparatus that includes a silicon substrate having a ***single*** porous microchannel formed therein. Paper No. 16, pages 4-5.

The Office asserts that Isaka only differs from the claimed invention "in failing to teach forming at least two porous microchannels in the silicon substrate." Paper No. 16, page 5.

The Office relies on Overton as disclosing that the gas chromatograph may include ***two*** different parallel columns, as depicted in FIG. 2(b) and discussed at column 9, lines 30-46. *Id.*

Independent claim 1 recites a sample separation apparatus that includes a substrate having matrices formed therein. The matrices comprise at least two distinct, unconnected porous regions that extend at least partially across the substrate. The sample separation apparatus of claim 1 also includes at least one detector fabricated on the substrate and associated with at least one of the at least two porous regions.

Independent claim 30 recites a separation apparatus comprising at least two distinct, unconnected capillary columns formed in a substrate, each of which comprises a porous matrix. The separation apparatus of claim 30 also includes a detector fabricated on the substrate and associated with at least one of the at least two porous regions.

Independent claim 51 recites a miniature chromatograph comprising a substrate having porous matrices, which have a plurality of pores, formed in the substrate that comprise at least two distinct, unconnected capillary columns.

Independent claim 64 recites an analyte detection apparatus comprising a silicon substrate with matrices formed therein, the matrices comprising at least two distinct, unconnected porous columns continuous with a surface of the silicon substrate.

The obviousness rejection of independent claims 1, 30, 51, and 64 is improper because the Office has not made the requisite showing of a suggestion or motivation in the evidence of record to select and combine the references as proposed. It is respectfully submitted that Applicant's own disclosure is the only evidence of record that suggests the desirability of the claimed invention. In each Office Action treating this rejection, the Office has made essentially the same statement concerning an alleged suggestion or motivation to combine the references as proposed, to wit:

> "Overton specifically taught that multiple columns in various configurations for different intended applications can be incorporated into miniaturized chromatograph devices suggesting that fabrication and use of multiple columns in separation chromatographs is well within ordinary skill." Paper No. 20, page 9; *see also* Paper No. 18, page 6; Paper No. 16, page 6.

Isaka does not teach or suggest the desirability of multiple porous silicon columns. Overton does not teach or suggest the desirability of chromatograph columns comprising porous silicon. Furthermore, the Office has not identified any other evidence of record supportive of a teaching, motivation, or suggestion to select and combine the references as proposed. Thus, it is respectfully asserted that the Office must be relying either on Applicant's own disclosure or some unarticulated general knowledge in the art in reaching the conclusion that the cited references should be selected and combined as proposed. These are improper bases for an obviousness rejection.

Although the Office never has explicitly identified a specific passage in Overton supportive of the above-quoted statement, Applicant believes the Office is referring to the statement in Overton that "[t]he basic design of the novel chromatograph allows a wide variety of specific instrument configurations, to fit particular intended uses" (Overton, col. 9, lines 30-32), to which the Office imputes an alleged suggestion that "fabrication and use of multiple columns in separation chromatographs is well within ordinary skill" (Paper No. 20, page 9). Applicant respectfully submits that this logical leap is unwarranted, particularly as it relates to the claimed invention. Overton's statement that his invention allows a wide variety of configurations suggests nothing with respect to the level of ordinary skill in the art of fabricating and using multiple column separation chromatographs. Overton is conspicuously silent as to chromatograph columns comprising porous silicon. Furthermore, while the above-quoted statement in Overton may be considered relevant to the reasonable expectation of success analysis, it is inapposite with respect to the analysis of a suggestion or motivation to select and combine the cited references as proposed. In other words, the fact that reference teachings ***can*** be combined does not equate with the requisite suggestion or motivation that they ***should*** be combined. What is lacking in the Office's obviousness case is a ***reason*** why one of ordinary skill would be motivated to combine the references as proposed.

The Office's attention is respectfully directed to FIG. 6 and the accompanying discussion in Overton, where it is plainly evident that Overton's discussion of chromatograph columns,

including the columns used in Overton's invention, refers to conventional tubular columns. Overton, FIG 6; col. 10, lines 24-25; col. 16, lines 35-36. Overton is silent as to the desirability or efficacy of chromatograph columns comprising porous silicon. Therefore, it is respectfully submitted that the statement in Overton the Office relies upon as a suggestion that it is "well within ordinary skill" to fabricate and use multiple columns can only refer to conventional tubular columns, not porous silicon columns. Applicant thus respectfully submits there is no teaching, suggestion, or motivation in Isaka or Overton (or any other evidence of record) to select and combine the references as proposed by the Office. Accordingly, it is respectfully submitted the Office has not established a *prima facie* case of obviousness with respect to the subject claims.

The obviousness rejection of independent claims 1, 30, 51, and 64 is also improper because there is no reasonable expectation of success. The Office asserts that one of ordinary skill in the art would have a reasonable expectation of success in incorporating the multiple columns of Overton into the miniaturized chromatograph apparatus of Isaka because Overton taught that multiple columns may be incorporated into chromatograph apparatuses. The Office alleges that this suggests that the use of multiple columns in chromatograph apparatuses is well within ordinary skill. Paper No. 18, page 6. However, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." *W.L. Gore & Associates, Inc. v. Garlock, Inc.,* 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 851 (1984).

When considered in its entirety, Overton includes a teaching that its columns are interconnected to facilitate the selection of the column through which the sample is conveyed. Overton, FIG. 2(b); col. 9, line 43 through col. 10, line 18. Therefore, any modification of Isaka to include the teachings of Overton would include interconnected columns. However, the matrices of the claimed invention are unconnected, porous regions and, therefore, are not interconnected. In addition, Overton discloses a multiple column apparatus having pneumatic valves at the interconnections between columns. The pneumatic valves of Overton could not be

used to interconnect porous columns formed in a silicon substrate. Overton thus teaches away from the claimed invention by teaching interconnected columns and by teaching pneumatic valves at the interconnections between columns.

The obviousness rejection of independent claims 1, 30, 51, and 64 is also improper because the cited references do not teach or suggest every limitation of the subject claims. Each of independent claims 1, 30, 51, and 64 recites a separation apparatus that comprises a substrate and matrices formed in the substrate. The matrices comprise at least two distinct, unconnected porous regions that extend at least partially across the substrate.

Neither Isaka nor Overton teaches or suggests that the matrices comprise two or more distinct, unconnected porous regions. Rather, Isaka teaches a chromatograph that includes a single, porous column formed in a silicon substrate and, therefore, does not disclose two or more distinct, unconnected porous regions. Overton teaches a gas chromatograph that includes interconnected, conventional tubular chromatography columns. Thus, the columns of Overton are not matrices formed in a substrate, nor do the columns of Overton include distinct, unconnected regions.

In summary, the Office has not established a *prima facie* case of obviousness with respect to independent claims 1, 30, 51, and 64 because the Office has not made particular findings, based on the evidence of record, as to the reason the ordinarily skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Lee,* 277 F.3d 1338 (Fed. Cir. 2002). The Office also has failed to establish a reasonable expectation of success of the proposed combination. Finally, the combination proposed by the Office does not teach or suggest all the limitations of independent claims 1, 30, 51, and 64. Therefore, independent claims 1, 30, 51, and 64 are not obvious, and claims 3-5, 7, 9-11, 13, 16, 18-20, 25, 29, 31-32, 34, 38, 39, 43, 46, 48-50, 52-53, 56, 69-71 and 73 depending therefrom are likewise not obvious. *In re Fine,* 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Isaka in View of Overton and Further in View of Swedberg

Claims 27, 28, 36, 37, 67 and 68 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 above, and further in view of U.S. Patent 5,571,410 to Swedberg et al. (hereinafter "Swedberg"). Applicant respectfully traverses the rejection, as set forth hereinafter.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton allegedly teach all the limitations of the subject claims except the use of antibody or antigen as the capture substrate for the miniaturized chromatograph. Paper No. 16, page 13.

The Office relies on Swedberg as teaching a miniaturized planar column device for integrated sample analysis of analytes. Paper No. 16, page 13. The Office states that Swedberg specifically teaches a stationary phase (sample treatment component) which performs a filtration function filled with a biocompatible porous medium of particles into which a capture function has been incorporated. *Id.* The Office further states that Swedberg teaches a stationary phase incorporated into a miniaturized affinity chromatography column onto which separation and capture functions are combined; the capture species (biological affiants) include antibodies, antigens, lectin, enzyme, etc. *Id.* Finally, the Office states that Swedberg also discloses a "LIGA" process which is used to refer to a process of fabricating microstructures having high aspect ratios and increased structural precision in order to create desired uniformity in microstructures such as channel ports, apertures, and microalignment means. *Id.*

The proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 27, 28 (dependent from independent claim 1), 36, 37 (dependent from independent claim 30), 67 and 68 (dependent from independent claim 64) are not obvious. *See In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Further, it is respectfully submitted that the open channel, porous material-filled, substrate-bound column of Swedberg does not cure the deficiencies discussed above in relation to the proposed combination of Isaka and Overton. Specifically, Swedberg does not provide any suggestion or motivation to combine the single, substrate-bound porous column of Isaka with the multiple, interconnected conventional columns of Overton to produce the invention recited in claims 27, 28, 36, 37, 67 and 68, provide a reasonable expectation that the combination of references would be successful, or teach or suggest the claim limitations that are lacking from the combination of Isaka and Overton. Since Swedberg does not cure the previously discussed deficiencies, claims 27, 28, 36, 37, 67 and 68 are not obvious over the combination of Isaka, Overton, and Swedberg. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claims 27, 28, 36, 37, 67 and 68 is respectfully solicited.

Isaka in View of Overton and Further in View of Miura

Claims 14, 15, 17, 21, 40, 41, 44, 54 and 55 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69, 71 and 73 above, and further in view of U.S. Patent 5,132,012 to Miura et al. (hereinafter "Miura"). Applicant respectfully traverses the rejection, as set forth hereinafter.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton allegedly teach all the limitations of the subject claims except for incorporating a field effect transistor detector, memory device, and controls in the apparatus. Paper No. 16, page 6.

The Office relies on Miura as disclosing:

> "a miniaturized sample separator in the form of a liquid chromatograph comprising an analyzing chip in which the capillary flowpath is formed in a substrate and a field effect transistor detector disposed downstream of the capillary. The substrate is made of silicon and further has an insulative membrane formed of silicon dioxide. Both the column for separation and the field effect

> transistor detector are formed integrally with the substrate. After the silicon oxide layer has been formed on the capillary groove, a stationary phase is formed. A valve is connected to a first end of the flow path in the sample application area (sample introduction pipe) where a sample is selectively introduced into the flow path. A separation carrier solution (carrier gas/vacuum source) is fed under pressure by a feed pump and then discharged from a drain after having passed through the flow path. Miura *et al.* further teach a sealing element (seal plate) such as borosilicate glass for sealing the opening portion of the groove portion to define the flow passage for a liquid sample. The liquid chromatograph also comprise[s] a memory (control) device and an output device such as a data processor which is connected to the detector for detecting separated constituents. Figures 4A and 4B illustrate an electrical conductivity detector which comprise[s] voltage application and current detection components, i.e. electrodes. Figure 9 shows a schematic view of the overall flow passage of the liquid chromatograph." Paper No. 16, pages 6-7.

The proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 14, 15, 17, 21 (dependent from independent claim 1), 40, 41, 44 (dependent from independent claim 30), 54 and 55 (dependent from independent claim 51) are not obvious. *See In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

Claims 17 and 44 are also allowable because the combination of Isaka, Overton, and Miura, as proposed by the Office, does not teach or suggest a memory device ***on a substrate*** of the chromatographs, as recited in the subject claims. Isaka does not teach or suggest any memory device. While Overton and Miura teach using memory devices with the columns that are taught therein, Miura teaches that its memory device is separate from the substrate by which the column is carried and positioned downstream of the column. Overton likewise teaches a memory device which is separate from the conventional tubular columns thereof.. Neither Overton nor Miura teaches a memory ***on the substrate*** of the chromatograph apparatus.

The Office asserts that since Overton and Miura do not specifically exclude the possibility that the memory device is disposed on the substrate, the memory device could, in fact, be disposed on the substrate. However, this assertion does not amount to a teaching or

suggestion that the memory device is located on the substrate. The Office certainly has not made any showing that either Overton or Miura teaches or suggests a memory device that is located ***on the substrate***. In addition, the Office's proposed combination disregards the fact that Miura and Overton both teach that memory devices are separate from the separation devices taught therein. Applicant respectfully submits that if the inclusion of a memory device on the substrate of a sample separation apparatus is an obvious design choice, the Office should cite a reference that discloses a sample separation apparatus with a memory device ***on the substrate***, as recited in claims 17 and 44.

Claims 21 and 41 are further allowable because the proposed combination of Isaka, Overton, and Miura does not teach or suggest a vacuum source in operative communication with a porous region. Neither Isaka nor Overton includes any teaching or suggestion of a vacuum source in communication with a porous region, which would be analogous to the columns thereof. The teachings of Miura are limited to the use of positive pressure to facilitate the movement of a sample through the column. Miura, col. 10, lines 1-34.

While the Office asserts that claims 21 and 41 do not exclude positive pressure, the fact remains that none of Isaka, Overton, nor Miura teaches or suggests that a vacuum source may be operatively communicate with a column thereof. It is difficult to conceive how the recitation of a vacuum source, as in claims 21 and 41, which is inherently a source of negative pressure, can be taught by a reference that merely teaches positive pressure. Thus, it is respectfully submitted the proposed combination fails to teach all the limitations of the subject claims.

It is also respectfully submitted that the single, substrate-bound open column of Miura does not cure the deficiencies discussed above in relation to the proposed combination of Isaka and Overton. Specifically, Miura does not provide any suggestion or motivation to one of ordinary skill in the art combine the single, substrate-bound porous column of Isaka with the multiple, interconnected, conventional tubular columns of Overton to produce the invention recited in any of claims 14, 15, 17, 21, 40, 41, 44, 54, or 55. Nor would one of ordinary skill in the art have a reasonable expectation that the proposed combination of references would be

successful, nor does the proposed combination teach or suggest the all limitations of the subject claims. Applicant therefore respectfully submits that claims 14, 15, 17, 21, 40, 41, 44, 54 and 55 are not rendered obvious by the combination of Isaka with Overton and Miura. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of these claims is respectfully solicited.

Isaka in View of Overton and Further in View of Wang

Claims 21 and 41 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 above, and further in view of U.S. Patent 5,663,488 to Wang et al. (hereinafter "Wang"). Applicant respectfully traverses the rejection, as set forth hereinafter.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton allegedly teach all the limitations of the subject claims except for integration of a migration facilitator into the separation chromatograph. Paper No. 16, page 8.

The Office relies on Wang as teaching:

> "a migration facilitator (pumping assembly) incorporated into a separation column and thermal device for use in selective control of thermal isolation of the thermal zone as well as effecting selective amount of gas pressure in an enclosed cavity. The pumping element comprises an element in the form of a tubular or planar palladium structure. Wang *et al.* disclose that the migration facilitator controls the extent of thermal isolation by changing the gas pressure in the cavity thereby changing the amount of heat transfer between the separation column and housing so as to reduce the need for operation of the thermal device. The migration facilitator also includes a control (check) valve for venting or purging gasses from the closed cavity, a vacuum (or near vacuum) source for use in high vacuum pumps for altering the concentration of gas within the cavity volume. Wang further disclose that a thermal conductivity detector is integrated into the chromatograph for determining physicochemical properties of the fluid stream which exits the separation column." Paper No. 16, pages 8-9.

The proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 21 (dependent from independent claim 1) and 41 (dependent from independent claim 30) are not obvious. *See In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

It is respectfully submitted that the conventional gas chromatograph use in connection with the device taught in Wang does not cure the deficiencies discussed above in relation to the proposed combination of Isaka and Overton. Specifically, Wang does not provide any additional suggestion or motivation to combine the single, substrate-bound porous column of Isaka with the multiple, interconnected, conventional tubular columns that are taught in Overton to produce the invention recited in claims 21 and 41, provide a reasonable expectation that the combination of Isaka and Overton would be successful, or teach or suggest the claim limitations that are lacking from the combination of Isaka and Overton.

Claims 21 and 41 are further allowable because the proposed combination of Isaka, Overton, and Wang does not teach a vacuum source operatively in communication with an end of the chromatography column. In contrast to the vacuum sources recited in claims 21 and 41, which are in operative communication with a porous region, the vacuum of Wang is used to vary the pressure within a chamber in which the column has been placed. Wang, col. 1, line 63 through col. 2, line 4; col. 2, lines 29-41. Therefore, the vacuum source of Wang is not in operative communication with the column. It is, therefore respectfully submitted the proposed combination does not teach or suggest all the limitations of the subject claims.

It is, thus, respectfully submitted that the proposed combination of Isaka, Overton, and Wang does not render claim 21 or claim 41 obvious under 35 U.S.C. § 103(a). It is, hence, respectfully submitted the Office has not established a *prima facie* case of obviousness with respect to the subject claims. Accordingly, withdrawal of the 35 U.S.C. § 103(a) rejection of claims 21 and 41 is respectfully solicited.

Isaka in View of Overton and Further in View of Northrup

Claims 22-24 and 42 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 above, and further in view of U.S. Patent 5,882,496 to Northrup et al. (hereinafter "Northrup"). Applicant respectfully traverses the rejection, as set forth hereinafter.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton allegedly teach all the limitations of the subject claims except for the migration facilitator comprising electrodes disposed into the porous region of the chromatograph. Paper No. 16, page 11.

The Office relies on Northrup as teaching:

> "fabrication and use of porous silicon structures to increase surface area of miniaturized electrophoresis devices and filtering or control flow devices. Northrup *et al.* specifically disclose that porous silicon which is fabricated from crystalline silicon have very small pore diameters so that they can be produced with relatively high degree of uniformity and control. Northrup *et al.* teach that because of its high surface area and specific pore size, porous silicon can be utilized for a variety of applications on a miniature scale for significantly augmenting adsorption, vaporization, desorption, condensation, and flow of liquids and gasses while maintaining the capability of modification such as being dopes or coated using conventional integrated circuit and micromachining. Electrodes within or adjacent the porous membrane can be used to control flow or electrically charged biochemical species such as in electrophoresis. Figure 3 illustrates porous silicon embodiment on a controlled flow interface device. Figure 8 illustrates a porous silicon electrophoresis device. A negative electrode is formed at one end (inlet) of the porous silicon column and a positive electrode is formed at an opposite end (outlet) of porous silicon columns, thereby forming microelectrophoresis channels." Paper No. 16, pages 11-12.

The proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons

stated above. Thus, claims 22-24 (dependent from independent claim 1) and 42 (dependent from independent claim 30) are not obvious. *See In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

It is respectfully submitted that the multiple, disconnected, substrate-bound porous columns of Northrup do not cure the deficiencies discussed above concerning the proposed combination of Isaka and Overton. Specifically, Northrup does not provide any suggestion or motivation to one of ordinary skill in the art to combine the single, substrate-bound porous column of Isaka with the multiple, interconnected, conventional tubular columns of Overton, provide a reasonable expectation that the combination of Isaka and Overton would be successful, or teach or suggest the claim limitations that are lacking from the combination of Isaka and Overton. Therefore, it is respectfully submitted that the proposed combination of Isaka, Overton, and Northrup does not render any of claims 22-24 or 42 obvious. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection of claims 22-24 and 42.

New Rejection: Isaka in View of Overton and Further in View of Swedberg

Claims 8, 26, 35 and 66 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 above, and further in view of Swedberg. Applicant respectfully traverses the rejection, as set forth hereinafter.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton allegedly teach all the limitations of the subject claims except for a capture substrate disposed on the porous region comprising a capillary column. Paper No. 20, page 5.

The Office relies on Swedberg as teaching:

> "a miniaturized planar column device for use in chromatographically or electrophoretically separating and analyzing analytes in a mobile phase. Swedberg *et al.* specifically disclose that the device has a stationary phase having porosity incorporated thereto (sample treatment component) which performs a filtration function filled with a biocompatible porous medium of particles into

> which a capture function has been incorporated therein. The capture substrate comprises antigens (biological affiant), antibody, lectin, enzyme substrate, capture oligonucleotide, etc. Swedberg *et al.* also disclose that each miniaturized column has a detector disposed proximate a detection region. The device allows a variety of drawing (injection or motive force) methods including application of differential pressure (pressure injection), capillary action (hydrodynamic injection), and electrical current (electrokinetic injection or electroosmotic flow). Swedberg *et al.* also disclose a "LIGA" process wherein microstructures having high aspect ratios and increased structural precision and uniformity in channels ports, apertures, and microalignment means are fabricated into the device. In Example I, Swedberg *et al.* exemplify separation and determination of imunoglobulins wherein assay and detection reagents are incorporated into the device during analysis." Paper No. 20, page 5.

The proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 8, 26 (dependent from independent claim 1), 35 (dependent from independent claim 30), and 66 (dependent from independent claim 62) are not obvious. *See In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

As indicated previously herein, Swedberg does not cure the deficiencies discussed above concerning the proposed combination of Isaka and Overton. Withdrawal of the rejection is, hence, respectfully solicited.

New Rejection: Isaka in View of Overton and Further in View of Northrup and Sunzeri

Claims 6, 57-62 and 72 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Isaka in view of Overton, as applied to claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73, and further in view of Northrup and U.S. Patent 5,536,382 to Sunzeri (hereinafter "Sunzeri"). Applicant respectfully traverses the rejection, as set forth hereinafter.

The teachings of Isaka and Overton, as relied upon by the Office, are as discussed hereinbefore. As relied upon by the Office, Isaka and Overton allegedly teach all the limitations

of the subject claims except for an electrophoretic apparatus comprising porous silicon columns and incorporating a control column into a separation device comprising porous silicon. Paper No. 20, page 7.

The Office relies on Northrup as teaching:

> "fabrication and use of porous silicon structures to increase surface area of miniaturized electrophoresis devices and filtering or control flow devices. Northrup *et al.* specifically disclose that porous silicon which is fabricated from crystalline silicon have very small pore diameters so that they can be produced with relatively high degree of uniformity and control. Northrup *et al.* teach that because of its high surface area and specific pore size, porous silicon can be utilized for a variety of applications on a miniature scale for significantly augmenting adsorption, vaporization, desorption, condensation, and flow of liquids and gasses while maintaining the capability of modification such as being doped or coated using conventional integrated circuit and micromachining. Electrodes within or adjacent the porous membrane can be used to control flow or electrically charged biochemical species such as in electrophoresis. Figure 3 illustrates porous silicon embodiment on a controlled flow interface device. Figure 8 illustrates a porous silicon electrophoresis device. A negative electrode is formed at one end (inlet) of the porous silicon column and a positive electrode is formed at an opposite end (outlet) of porous silicon columns, thereby forming microelectrophoresis channels." Paper No. 20, page 7.

The Office relies on Sunzeri as teaching:

> "analysis of constituents of human biological fluids using capillary electrophoresis. Sunzeri specifically teaches the use of standard control to provide a standard for quantitation. Sunzeri further teaches that quantitation using internal and external standards is beneficial in assays where the sample matrix affects fluorescence sample quenching." Paper No. 20, page 8.

The proposed combination of Isaka and Overton does not render claims 1, 3-5, 7, 9-11, 13, 16, 18-20, 25, 29-32, 34, 38, 39, 43, 46, 48-53, 56, 64, 69-71 and 73 obvious for the reasons stated above. Thus, claims 6 (dependent from independent claim 1) and 72 (dependent from independent claim 64) are not obvious. *See In re Fine*, 837 F.2d 1071 (Fed Cir. 1988).

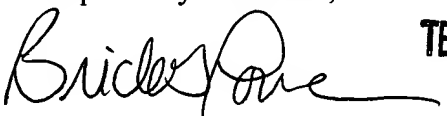
It is respectfully submitted that neither the multiple, substrate-bound, porous columns of Northrup nor the electrophoretic-media-filled capillary tubes used in Sunzeri cures the deficiencies discussed above concerning the proposed combination of the single, substrate-bound porous column of Isaka and the multiple, interconnected, conventional tubular columns of Overton. Furthermore, the Office makes no attempt to identify any suggestion or motivation in any of the references to select and combine Isaka, Overton, Northrup, and Sunzeri, as proposed. Accordingly, the Office has not established a *prima facie* case of obviousness with respect to the subject claims. Withdrawal of the 35 U.S.C. § 103(a) rejection of claims 6 and 72 is, therefore, respectfully solicited.

## CONCLUSION

Reconsideration is respectfully requested. It is respectfully submitted that claims 1, 3-11, 13-44, 46, 48-64, 66-74 and 105-107 are allowable over the cited references. Therefore, Applicant respectfully solicits the allowance of claims 1, 3-11, 13-44, 46, 48-64, 66-74 and 105-107 and an early notice of the same. Should issues remain after consideration of the foregoing that may be resolved most expeditiously by a telephonic conference, the Office is kindly requested to contact Applicant's undersigned representative.



Respectfully submitted,



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